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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/573,232	03/23/2006	Philippe G. Nantermet	21546YP	5429

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EXAMINER	
WARD, PAUL V	
ART UNIT	PAPER NUMBER
1624	

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10/26/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/573,232	NANTERMET ET AL.	
	Examiner	Art Unit	
	PAUL V. WARD	1624	

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,12-19,21 and 23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-9,12-19 and 21* is/are allowed.

6)☒ Claim(s) *23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/23/06 3/23/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on September 22, 2008 is acknowledged. The traversal is on the ground(s) that the unity of invention requirement is met by the structure shown in Figure I. This is not found persuasive because The inventions listed as Groups I-XX do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Group I is drawn to a compound, its composition and method of use. Group II is a different compound with respect to the compound of Group I. Therefore, there is no special technical feature for the compounds or different fields of application of the compounds. Additionally, there is no unity of invention.

There is no special technical feature, which unites the groups. But even if there were a special technical feature there must be unity of invention also. Under 37 CFR 1.475:

(a) An international and a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention"). Where a group of inventions is claimed in an application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features"

shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

(b) An international or a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories:

(1) A product and a process specially adapted for the manufacture of said product; or

(2) A product and a process of use of said product; or

(3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or

(4) A process and an apparatus or means specifically designed for carrying out the said process; or

(5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

The above groups 1-2 together do not meet the requirement of unity of invention as given above in (1) -(5).

The requirement is still deemed proper and is therefore made **FINAL.**

Applicant is entitled to have the method Groups rejoined under M.P.E.P. § 821.04, if the claims of Group I are ultimately found allowable.

Groups II-XX are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement, and reserved the right to file a divisional application to the non-elected subject matter.

An action on the merits on claims 1-9, 12-19, 21 and 23 is contained herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 23 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 23 is directed to a method of treating Alzheimer's disease. The term is interpreted to include any and all forms Alzheimer's disease including inhibiting gamma secretase and deposition of beta amyloid protein. In light of this, it can be asserted that in spite of the vast expenditure of human and capital resources in recent years, no one drug has been found which is effective in treating all types/forms of Alzheimer's disease. In re Hozumi, 226 USPQ 353 (ComrPats 1985).

The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations. In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include, but are not limited to:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims

The breadth of the instant claims is seen to encompass methods for treating of Alzheimer's disease by administering to a patient in need of such treatment a therapeutically effective amount of the compound claim. Applicant failed to exactly defined how Alzheimer's disease, inhibiting gamma secretase and deposition of beta amyloid protein are treated. Thus, the claim is extremely broad.

The nature of the invention

The nature of the invention is the treatment of Alzheimer's and through the use of the claimed compound and derivatives thereof. Currently, there are no known agents that treat Alzheimer's including inhibiting gamma secretase and deposition of beta amyloid protein all inclusively.

The level of predictability in the art

The treatment of Alzheimer's is highly unpredictable. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

The amount of direction provided by the inventor.

The applicant has not demonstrated sufficient guidance provided in the form of administration profiles, combination ratios of the active agents or reference to the same in the prior art to provide a skilled artisan with sufficient guidance to practice the instant treatment of Alzheimer's claimed. Further, the applicant discloses that an effective amount of the compound will be administered (see specification) without providing any direction other than that the compounds of the invention have a high therapeutic index and follows this with a definition readily found in a basic pharmacology textbook. It should be noted that the therapeutic index of a drug in humans is almost never known and is only determined through clinical experience.

The existence of working examples.

There is not seen in the disclosure, sufficient evidence to support Applicant's claims of treating Alzheimer's. A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 27 USPQ2d 1510 (CAFC). The disclosure does not demonstrate sufficient evidence to support the applicant's claim to the treatment and methods in inhibition. There are not sufficient working examples or data from references of the prior art to provide a nexus between those examples and a method of treating with the claimed compound.

The level of one of ordinary skill.

The level of skill is that of one with a doctoral understanding of Alzheimer's and neurodegenerative diseases therapeutics. Applicants claim a method of treatment for Alzheimer's disease, this disease is a very hard to treat. The central characteristic of Alzheimer's disease is the deficiency in the level of the neurotransmitter Acetylcholine that plays an important role in memory. Alzheimer's Disease is an extraordinarily difficult disease to treat, and has been the subject of a vast amount of research. Despite an enormous number of different approaches, the skill level in the art is so low relative to the difficulty of task that the only success has come from treatment by compounds such as Acetylcholinesterase inhibitors (Aricept®, Cognex®, Exelon®, and Reminyl®), a property not disclosed in Applicant's compounds.

Furthermore, there is no evidence that the inhibition of amyloid B-peptide production for the treatment of Alzheimer's disease has ever been accomplished. For example, Golde teaches that at least one group has used gamma-secretase inhibitors in an animal model to lower the levels of B-amyloid in the brain and that at lease one gamma-secretase inhibitor has gone to clinical trials. (See J. Clin. Invest. 111:11-18 (2003) at page 13). However, Golde makes clear that the actual treatment of the condition of Alzheimer's based upon inhibition of gamma-secretase is still being developed and that identification of an inhibitor is not enough. Golde also lists several problems with regard to undesirable pleitropic effects that must be addressed prior to development of an actual treatment. (See page 13, col. 2). Applicant's system fails to address the problems of undesirable pleitropic effects, and thus, it appears that while gamma-secretase may be a viable drug target in the future, considerable future

research needs to be done. In view of the Golde reference, Applicant's data is not convincing as to make the production and use of pharmaceutical compositions comprising the recited compounds feasible without undue, un-predictable experimentation.

The quantity of experimentation.

A great deal of experimentation is required. In order for there to be a method of treating Alzheimer's disorders generally, as claimed by the applicant, it would be necessary to show that a vast range of different types of Alzheimer's and neurodegenerative. Furthermore, direction, in the form of examples, must be shown to determine what an effective dose may be. The references submitted do not demonstrate this. Therefore, one of ordinary skill in the art would require a significant amount of experimentation in order to determine the effective dosage to treat the multitudes of different types of Alzheimer's and neurodegenerative diseases with the claimed compound individually or in combination with other therapeutic agents. Moreover, in view of the level of one of ordinary skill, since the inhibition of Aβ-peptide production for the treatment of Alzheimer's disease has never been accomplished, no guidance from the success of others is available from this experimentation.

Thus, it can be safely concluded that the instant case fails to provide an enabling disclosure for the treatment of Alzheimer's disease.

Allowable Subject Matter

Claims 1-9, 12-19 and 21 are allowed. The prior art does not teach any of the benzylether and benzylamino compounds of Group I, wherein R_1 is phenyl or napthyl, substituted in the manner claimed by the Applicant. Thus, the compounds in Group I were neither found to be obvious nor anticipated by the prior art of record. The prior art does not teach or suggest the presently claimed compound.

Conclusion

Claims 1-9, 12-19, 21 and 23 are pending. Claim 23 is rejected. Claims 1-9, 12-19 and 21 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL V WARD whose telephone number is 571-272-2909. The examiner can normally be reached on M-F 8 am to 4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/PAUL V WARD/
Examiner, Art Unit 1624

/James O. Wilson/
Supervisory Patent Examiner, Art Unit 1624